AmBisome® Phase III Study For Cryptococcal Meningitis

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Data Suggest Equivalent Efficacy and Improved Safety Profile for

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Fujisawa Healthcare, Inc. (Fujisawa) and Gilead Sciences, Inc. (Nasdaq: GILD) today presented results from a Phase III clinical study comparing the safety and efficacy of AmBisome (liposomal amphotericin B) to conventional amphotericin B for the initial treatment of acute cryptococcal meningitis in AIDS patients. The study results indicate that AmBisome is as effective as amphotericin B, yet appears to be significantly less toxic.

The results are being publicly presented for the first time by Richard J. Hamill, MD, Associate Professor, Departments of Medicine and Microbiology/Immunology, Baylor College of Medicine, VA Medical Center, Houston, Texas, during an oral presentation at 3:15 p.m. on Monday, September 27th in Room 304 at the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco, California.

In this double-blind comparison study, a total of 267 AIDS patients received either AmBisome at 3 mg/kg (86 patients), AmBisome at 6 mg/kg (94 patients) or conventional amphotericin B at 0.7 mg/kg (87 patients) daily for 14 to 21 days as induction therapy for acute cryptococcal meningitis. Patient demographics and other baseline characteristics were comparable between groups. Mean induction treatment durations were 13.5, 14.0 and 13.3 days, respectively.

AmBisome 3 mg/kg and 6 mg/kg demonstrated efficacy equivalent to conventional amphotericin B for all endpoints, including two week culture conversion (63.3%, 53.7% and 53.7% respectively), two week clinical response (65.8%, 75.3% and 65.8%) and two week survival (90.7%, 94.7% and 89.7%).

AmBisome was associated with significantly fewer infusion-related reactions compared to conventional amphotericin B. Specifically, the data indicate that patients receiving either AmBisome 3 mg/kg or 6 mg/kg experienced significantly fewer chills/rigors (5.8%, 8.5% versus 48.3%; $p<0.001$ and $p<0.001$), fever (7.0%, 8.5% versus 27.6%; $p<0.001$ and $p<0.001$) and respiratory problems (0%, 1.1% versus 9.2%; $p=0.007$ and $p=0.015$) as compared to the patients treated with conventional amphotericin B. In addition, the incidence of nephrotoxicity as defined by a doubling of baseline serum creatinine was lower in the AmBisome groups compared with conventional amphotericin B (14.0%, 21.3% and 33.3%; $p=0.004$ and $p=0.066$). The incidence of liver dysfunction was similar between treatment groups.

“Cryptococcal meningitis in AIDS patients is extremely serious. Your primary treatment goal is to save lives,” said Dr. Hamill, MD, lead investigator of the Phase III trial. “To have a medication with comparable efficacy to the standard of care that so substantially reduces side effects could allow physicians to help improve the quality of care for this vulnerable patient population.”

Based on the study results, Fujisawa submitted a Supplemental New Drug Application (sNDA) for the anti-fungal agent AmBisome to the U.S. Food and Drug Administration (FDA) on July 6, 1999, for the treatment of cryptococcal meningitis in AIDS patients.

AmBisome is co-marketed in the United States by Fujisawa Healthcare, Inc. and Gilead Sciences. It is currently indicated for the treatment of confirmed infections caused by various fungal species or visceral leishmaniasis, a parasitic infection. AmBisome is the first and only amphotericin B product cleared for marketing by the U.S. FDA for empiric therapy for presumed fungal infections in patients with low white blood cell counts and who exhibit fever of unknown origin. Additionally, AmBisome is available for the treatment of systemic fungal infections in 38 countries worldwide.

“We are strongly encouraged by the outcome of this important clinical study. We look forward to the FDA’s comprehensive review of the data which we believe shows that AmBisome provides an effective and safer alternative to conventional amphotericin B therapy in the treatment of this life-threatening illness,” stated Ira D. Lawrence, MD, Vice President of Research and Development at Fujisawa.

Additional Data Indicate AmBisome is Well Tolerated at High Doses

Data from another study presentation at ICAAC suggest AmBisome doses of as much as 15 mg/kg/day are well tolerated and can provide effective therapy for aspergillosis and other filamentous fungal infections. The Phase I/II dose escalation trial included 44 patients assigned to doses of AmBisome 7.5 (n=8), 10.0 (n=10), 12.5 (n=7) or 15.0 (n=19) mg/kg/day. AmBisome was well tolerated at all doses without any dose-limiting toxicities. Twenty-one patients had proven or probable fungal infection (13 aspergillosis, 5 zygomycosis and 3 fusariosis). Infusion- related reactions on Day 1 consisted of fever in 8 patients and rigors/chills in 5 patients. A doubling of baseline serum creatinine occurred in 32% of all patients but was not dose-related.

This Phase I/II study will be presented by Thomas Walsh, MD, of the National Cancer Institute, National Institutes of Health at the poster session entitled "Management of Fungal Infections in Man" on Tuesday, September 28, 1999.

About Fujisawa and Gilead

Fujisawa Healthcare, Inc., headquartered in Deerfield, Ill., develops, manufactures, and markets proprietary pharmaceutical products in the United States and abroad. Fujisawa Healthcare, Inc., is a subsidiary of Fujisawa Pharmaceutical Co., Ltd., based in Osaka, Japan. Fujisawa Pharmaceutical Co., Ltd., founded in 1894, is a leading pharmaceutical manufacturer and is actively developing its international operations in North America, Europe and Asia. Additional information on Fujisawa Healthcare, Inc., and its products can be found on the Internet at http://www.fujisawa.com.